

Scientific abstract for protocol "Adenovirus p53 Infected DC Vaccine for Breast Cancer".

Breast cancer is the most common cancer and the second leading cause of cancer deaths in women. The prognosis for patients with breast cancer is dependant on the stage of disease at diagnosis and even women with disease localized to the breast and axillary nodes are at risk of relapse. Surgery and adjuvant therapy with chemo, hormonal, and radiation therapy reduce the risk of relapse; however, 30-70% of patients with stage II and III breast cancer will relapse and die. Immune mediated therapies provide one adjuvant strategy and vaccines with breast cancer associated antigens are a promising approach. P53 is an attractive antigen, as 50% of breast cancer patients have tumors with p53 expression and 68% of women with 4 or more positive nodes have p53 mutations. Based on our prior studies demonstrating the ability of adenovirus (Adv) to efficiently infect hematologic cells, we will use adenovirus-p53 to infect dendritic cells (DCs) as our vaccine. Our laboratories and others have shown that DC based vaccines can augment cytotoxic T lymphocyte responses and in translational studies to provide therapeutic activity. However, the efficacy of vaccines when administered in combination with cytoreductive therapy and the role of the timing of administration on the immune response is not clear. Thus, one critical question is should vaccination occur early during primary induction therapy, before T cell polyclonality is lost or should it be initiated following primary therapy when the remaining T cells are no longer subject to cytoreductive therapy? Therefore, in these prospectively randomized studies we will directly compare p53 immunization during "chemotherapy recovery periods" in the induction protocol, with p53 vaccination immediately following primary therapy. The hypothesis to be studied is that vaccination with adenovirus-p53 transfected DC can induce a p53 specific T cell response, the extent of which is dependant on the timing of immunization relative to primary therapy. In these studies, we will determine the toxicity and immune augmentation to p53 and Adv by vaccination with Adv-p53 transfected DC in stage II and III breast cancer patients. In addition we will assess the importance of vaccine timing relative to cytotoxic therapy on the augmentation of antigen specific immune responses and the effect of cytotoxic therapy on innate immunity.